

Docket No.: G0744.70042US07
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Katherine Gordon et al.
Serial No.: 07/839,194
Confirmation No.: 6108
Filed: February 20, 1992
For: TRANSGENIC ANIMALS SECRETING DESIRED PROTEINS INTO MILK
Examiner: D. A. Montanari
Art Unit: 1632

SECOND DECLARATION OF HARRY M. MEADE

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Harry M. Meade, declare that:

1. I am the Senior Vice President of Research and Development with GTC Biotherapeutics, Inc., the exclusive licensee of the present application, which is a company I joined in 1993 and of which I am a founding member. I direct all transgenic molecular biology research and development efforts conducted within GTC Biotherapeutics, Inc., including the evaluation of technologies having the potential to increase the efficiencies of transgenic protein expression.

2. I have over 25 years of research experience, the last at least fifteen years pertaining to transgenic research and the development of protein expression systems. I have been recognized as a pioneer in the field.

3. I have also held scientific positions with Genzyme Corporation, Biogen and Merck. I received my Ph.D. in Biology from the Massachusetts Institute of Technology and completed post-doctoral studies at Harvard University. Further details of my education and research experience, including lists of my publications, patents and lectureships, are found in my *curriculum vitae* (Exhibit N).

4. I make this declaration in support of the above-referenced patent application and in response to the Office Action of December 4, 2008. I understand that this application was filed on February 20, 1992 and claims priority to an application filed on April 9, 1986.

5. While the classification varies somewhat in the art, generally, there are seven types of proteins in the genus of mammalian milk proteins, and this genus can be divided into subgenera: the milk serum proteins (whey acid protein (WAP), alpha-lactalbumin and beta-lactoglobulin) and the casein proteins (alpha, beta, kappa and gamma casein).

6. The promoters of all of the above-mentioned milk serum proteins and of casein proteins have been used to express foreign genes. See Maga and Murray (1995), *Mammary Gland Expression of Transgenes and the Potential for Altering the Properties of Milk*, Bio/Technology, Vol. 13 (Exhibit K); Clark (1998), *The Mammary Gland as a Bioreactor: Expression, Processing, and Production of Recombinant Proteins*, Vol. 3, No. 3 (Exhibit L); Echelard and Meade (2003), *Protein production in transgenic animals*, Chapter 24, S.C. Makrides (Ed.) *Gene Transfer and Expression in Mammalian Cells* (Exhibit M).

7. The expression of foreign genes has been successful in a number of mammalian species, including mouse, goat, pig, sheep, rabbit and cattle. See Ibid.

8. As with all biological techniques and experimental methods, the level of expression may vary. However, the promoters of all of the above-mentioned milk serum proteins and of casein proteins have been successfully used, and I am not aware of a reason why they could not have been used successfully at the time the above-referenced application was filed by one skilled in the art exercising ordinary skill, including a reasonable amount of experimentation.

I, the undersigned, declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this document and any patent which may issue from the above-identified patent application.

6/3/09
Date

Harry M. Meade
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